PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The Effect Of Whole Body Vibration Exercise In Preventing Falls And Fractures: A Systematic Review And Meta-analysis
AUTHORS	Jepsen, Ditte; Thomsen, Katja; Hansen, Stinus; Jørgensen, Niklas; Masud, Tahir; Ryg, Jesper

VERSION 1 – REVIEW

REVIEWER	Feng Yang GSU, USA
REVIEW RETURNED	02-Jul-2017

GENERAL COMMENTS	Title: The effect of whole body vibration exercise in preventing falls and fractures: A systematic review and meta-analysis The authors retrieved and analyzed 14 RCT trials which examined the effect of whole body vibration training in reducing falls and strengthening bones in older adults. The findings are in favor that WBV reduces falls whereas it may not be effective to improve BMD or microarchitecture. This article has few strengthens, such as the inclusion of only RCT trials and its large sample size. However, few issues prevent the publication of this manuscript. 1. One concern is that the duration of interventions differs considerably among trials. How such a variation affects the finding and results needs to be addressed. Additionally, the authors stated that “only falls data from the intervention periods of the studies were extracted.” This raised another question that how the fall data collected in a very short duration (like weeks) is sufficiently powered to support the findings. It could be possible that no falls were captured for either group owing to the very short duration. Remember that the average fall rate is one out of three annually. 2. The manuscript summarized the vibration intensity in terms of the peak acceleration. It would be beneficial for the research community if the authors could seek if the vibration intensity correlates with the training effect. 3. The authors should be commended for acknowledging the largely different training protocol and design across studies. However, the authors did not discuss any potential influence of the variance in the vibration parameters/protocol design on the outcomes. Without providing this information, it remains inconclusive if WBV is effective and if so what would be the desired training parameters. 4. A detailed description of the exclusion of the 2141 articles should be given.

	5. Some studies' participants age is under 65 y/o. Justifications are needed for this. Otherwise, it may affect the external validity of this study. 6. Page 7, Line 43. What are the numbers inside the secondary-level parentheses?

REVIEWER	Eloá Moreira Marconi Universidade do Estado do Rio de Janeiro - Brazil
REVIEW RETURNED	15-Jul-2017

GENERAL COMMENTS	I was really grateful to participate in the review of this study. I would like to congratulate the authors and encourage them to continue their studies about benefits of WBVE.

REVIEWER	Judith Godin Nova Scotia Health Authority and Dalhousie University Canada
REVIEW RETURNED	23-Aug-2017

GENERAL COMMENTS	The content of this paper is outside my area of expertise and, therefore, I can only comment on the methodology and statistics. Overall, the authors clearly and comprehensively presented their methods and results. Appropriate analyses were used and sensitivity analyses were conducted when appropriate. I only have a couple of minor points. One of the inclusion criteria was adults aged 50 and older. Does this mean that studies were only included if every participant was over the age of 50? Were there any studies that has some or a majority of participants over the age of 50 which were excluded? Please clarify and comment if necessary. Please provide more informative figure captions so that the reader does not have to refer back to the text to know exactly was is represented in the figure.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

We thank the reviewer for the thorough review and the useful aspects.

Comment 1:

"One concern is that the duration of interventions differs considerably among trials. How such a variation affects the finding and results needs to be addressed. Additionally, the authors stated that "only falls data from the intervention periods of the studies were extracted." This raised another question that how the fall data collected in a very short duration (like weeks) is sufficiently powered to support the findings. It could be possible that no falls were captured for either group owing to the very short duration. Remember that the average fall rate is one out of three annually."

Answer 1:
We acknowledge the question about the duration of the intervention. The duration of the interventions differs considerably among the trials which can contribute to differences in effect sizes. We only extracted data from the intervention periods to ensure similarity enough to justify pooling of the results. In the meta-analysis the I2 statistics can be viewed as the quantity of the inconsistencies in the effect sizes among the studies (1). We found a low I2 in the falls calculations which can be viewed as low heterogeneity. I2 is higher for the bone parameters and therefore, in the cases where I2 is high the quality of the evidence is graded down in the summary of the evidence table (table 3), as recommended in the GRADE guidelines (1).
We have conducted a post hoc subgroup analysis showing the intervention longer than 6 months where WBV is associated with a greater effect in fall prevention. The effects on bone mineral density (BMD) have been analyzed according to duration by others in a recent meta-analysis (2).

The following changes has been made to the result section under falls page 14, section 2, line 5-10, and additional supplement data has been added (supplement data Figure 2a-c)

“Post hoc subgroup analyses were conducted to assess the association between the duration and the magnitude of the vibration and falls, duration over six months fall rate ratio of 0.61 (95% CI 0.47-0.80, p=0.0004, I2=0%, 2 studies), duration over six months and relative risk of experiencing falls of 0.61 (95% CI 0.47-0.80, p=0.0004, I2=0%, 2 studies), low magnitude vibration fall rate ratio of 0.56 (95% CI 0.40-0.78, p=0.0006, 1 study), high magnitude vibration fall rate ratio of 0.80 (95% CI 0.55-1.18, p=0.26, I2=0%, 2 studies) (supplement data Fig 2a-c). “

Comment 2:
“The manuscript summarized the vibration intensity in terms of the peak acceleration. It would be beneficial for the research community if the authors could seek if the vibration intensity correlates with the training effect.”

Answer 2:
The comment on the vibration intensity is highly relevant. The peak acceleration is a measure of the frequencies and amplitude. We conducted post hoc analyses according to vibration magnitude on three studies measuring falls and found no effect in a study with high magnitude vibration. However we found an effect in the two other studies, one with high magnitude, the other with low magnitude vibration. Overall we saw no clear dose-response correlation. The effect of the vibration intensity on BMD has recently been reported by others (2) and due to limited data on other bone parameters it is currently not possible to report if the vibration intensity in other bone parameters correlates with the training effect.

The added changes in answer 1 also reflect this, result section under falls page 14, line 5-10.

Comment 3:
“The authors should be commended for acknowledging the largely different training protocol and design across studies. However, the authors did not discuss any potential influence of the variance in the vibration parameters/protocol design on the outcomes. Without providing this information, it remains inconclusive if WBV is effective and if so what would be the desired training parameters.”

Answer 3:
We would like to thank the reviewer for the question about variance in vibration protocols. Vibration training can be conducted with different exercises on the plate, with focal vibration and with stochastic resonance vibration. In the systematic review we have investigated the effect of vibration exercise where the participants had to receive the training standing on the plates, excluding the focal vibration, and stochastic resonance vibration.

To insure comparable groups and isolate the effect of WBV the RCTs had to have vibration compared to controls with no intervention, sham or activities not influencing strength, balance or bone. Trials that had WBV in combination with resistance training also had to have a resistance training group only, which was used as control group to isolate the effect of the WBV.

In the submitted subgroup analysis figure 5-a we looked at vibration protocol parameters of vertical vibration and side-alternating vibration, and only small differences were found.

Following answer 1-3 we added the following changes to the discussion section under falls page 19, line 12-15.

“With the available data the analysis shows a fall reduction in the vibration groups with low heterogeneity and with the observational power of the post hoc subgroup analyses we found an association between studies with duration longer than 6 months and a larger reduction in falls.”

Comment 4:
“A detailed description of the exclusion of the 2141 articles should be given.”

Answer 4:
The exclusion of the 2141 articles were performed by the corresponding author in the Covidence review system by screening the titles and abstract to the inclusion and exclusion criteria written in the method section page 5, line 26-31, and page 6, line 1-6.

“Inclusion criteria: randomized controlled trials (RCT) investigating the effect of WBV on fractures, falls, and bone properties within the population ≥ 50 years of age. WBV had to be whole-body sinusoidal vibration (i.e. constant vibration frequency) from a platform that vibrates vertically or side alternating, with no restriction on frequency, amplitude, or magnitude. The participants had to stand during the WBV. The control groups had to have either no intervention, usual care, sham vibration, activity unlikely to influence bone or fall risk parameters, or exercise or interventions identical in both arms (where WBV was an add on in one group).
Trials were ineligible if non RCT, animal studies, population age < 50 years given by the mean age minus two times the standard deviation, or if the participants were younger than 50 years of age, non-English language publications, posters, or conference abstracts, and if vibration was applied locally, by electrical current, non-standing, with random frequencies, using vibrating insoles, or by ultrasound.”
We have no detailed data on how many abstract were excluded due to each specific exclusion criteria.
The judgment of the 106 full text papers were performed by two authors independently and the detailed description of this exclusion can be found in the Prisma flow chart figure 1.

Comment 5:
“Some studies’ participants age is under 65 y/o. Justifications are needed for this. Otherwise, it may affect the external validity of this study.”

Answer 5:
We would like to thank reviewer for the comment about the participant’s age in the study.
To be included in the study the mean age of the participants minus 2 times the standard deviation had to be above 50 years of age, and if the studies included participants under 50 they were excluded. The lower age limit of 50 was set in order to make sure we included all relevant studies with postmenopausal women looking at bone parameters and to ensure that all relevant studies measuring falls were included. The mean age of all the participants in the review was 74 years of age, reflecting a relevant age group for falls.

Comment 6:
“Page 7, Line 43. What are the numbers inside the secondary-level parentheses?”

Answer 6:
The standard deviation is obtained from the standard error of a mean by multiplying by the square root of the sample size
SD = SE * √n
We used the formula for calculating the Standard deviation from the 95% confidence interval for group means, using a t-distribution:
SD = ((HCI-LCI/2/TINV(0.05;n-1)*√ (n))
HCI= highest value of the 95% confidence interval
LCI= lowest value of the 95% confidence interval
TINV(0.05;n-1)= t value for a 95% confidence interval from a sample size of n

We have added the following changes in the method section page 7, line 13.

“Where HCI is the highest value of the 95% confidence interval, LCI is the lowest value of the 95% confidence interval, and n the sample size of the group, TINV(0.05;n-1)= t value for a 95% confidence interval from a sample size of n, as described in the Cochrane handbook of systematic reviews (36).”

Reviewer 2
Comment:
“I was really grateful to participate in the review of this study. I would like to congratulate the authors and encourage them to continue their studies about benefits of WBVE.”

Answer:
We are very grateful for the encouraging remark.

Reviewer 3

Comment 1:
“The content of this paper is outside my area of expertise and, therefore, I can only comment on the methodology and statistics. Overall, the authors clearly and comprehensively presented their methods and results. Appropriate analyses were used and sensitivity analyses were conducted when appropriate. “

Answer 1:
We thank reviewer for the comment on methodology and statistics

Comment 2:
“One of the inclusion criteria was adults aged 50 and older. Does this mean that studies were only included if every participant was over the age of 50? Were there any studies that has some or a majority of participants over the age of 50 which were excluded? Please clarify and comment if necessary.”

Answer 2:
Studies were excluded if the mean age minus 2x the standard deviation were below 50, or if the participants were younger than 50 years of age.

We identified and excluded a total of three studies which had a majority of participants above 50 years of age but did not meet the age criteria (1, 2, 3). Two studies found no effect on BMD (1, 2) in line with our results, one study found an effect on BMD (3), one study found a slight negative effect of WBV on ultrasound of the heel, and falls were measured as an adverse outcome (1) where WBV had a fall preventive effect in line with our results.

To clarify the inclusion age the following changes have been made in the method section page 6 line 2-3.

“Trials were ineligible if non RCT, animal studies, population age < 50 years given by the mean age minus 2 times the standard deviation, or if the participants were younger than 50 years of age, non-English language publications, posters, or conference abstracts, and if vibration was applied locally, by electrical current, non-standing, with random frequencies, using vibrating insoles, or by ultrasound.”

Comment 3:
“ Please provide more informative figure captions so that the reader does not have to refer back to the text to know exactly was is represented in the figure.”

Answer 3:
We would like to thank the reviewer for the comment on the figure captions. We have provided more informative figure captions in all the figures.

References
1. Schünemann H BJ, Guyatt G, Oxman A GRADE handbook for grading quality of evidence and strength of recommendations Updated October 2013. The GRADE Working Group
2. Oliveira LC, Oliveira RG, Pires-Oliveira DA. Effects of whole body vibration on bone mineral density in postmenopausal women: a systematic review and meta-analysis. Osteoporosis International . 2016;27(10):2913-33..
3. Slatkovska L, Alibhai SM, Beyene J, Hu H, Cheung AM. Effect of 12 months of whole-body vibration therapy on bone density and structure in postmenopausal women: a randomized trial. Ann Intern Med. 2011 Nov 15;155(10):668-79, W205.
4. Marin-Cascales E, Rubio-Arias JA, Romero-Arenas S, Alcaraz PE. Effect of 12 Weeks of Whole-Body Vibration Versus Multi-Component Training in Post-Menopausal Women. Rejuvenation Res. 2015;18(6):508-16.
5. Russo CR, Lauretani F, Bandinelli S, Bartali B, Cavazzini C, Guralnik JM, et al. High-frequency vibration training increases muscle power in postmenopausal women. 2003; 84(12):[1854-7 pp.].

VERSION 2 – REVIEW

REVIEWER	Judith Godin Nova Scotia Health Authority Canada
REVIEW RETURNED	18-Oct-2017

GENERAL COMMENTS	The authors have addressed my concerns.